

REMARKS

Claim 2 is amended to correct a typographical error, and the amendment does not narrow the scope of the claim.

Claims 4, 5, 9, and 10 are also amended, but do not narrow the overall scope of the claims taken together.

Rejection of claims 4 and 9 under 35 U.S.C. § 112, second paragraph

The claims were rejected for “failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention” because “specification lacks definition/criteria that defines said corticosteroid(s) as either a mid- or a high- potency corticosteroid.” Claims have been amended to be drawn toward specific corticosteroids.

This amendment does not narrow the broadest claims of the application.

Rejection of claims 1-11 under 35 U.S.C. § 103(a)

The Office Action alleges that the claims are obvious over Yamamoto ('906) and Nagpal ('279) in combination.

The Office Action continues to maintain that a prima facie case of obviousness has been made. Although Applicant does not necessarily agree, the prima facie case will not be addressed here. Rather, evidence of unexpected results will be established.

In the preliminary amendment, Applicant provided the Gollnik reference and took the position that the combination of tazarotene and a corticosteroid reduces the number of adverse events as compared to tazarotene alone. Applicant asserted that this result is unexpected. The Office Action rejected that position by noting that “the incidence of treatment related adverse events for tazarotene plus mid- or high-potency corticosteroid as taught by Gollnick is almost identical, i.e., 32% and 31% respectively. Thus Gollnik can not be seen as supporting the applicant’s assertion of unexpected results.” Applicant does not agree that comparison of the tazarotene/mid-potency corticosteroid with the tazarotene/high-potency corticosteroid is relevant to whether the number of adverse events would be greater for the combination therapies as compared to the individual monotherapies. Applicant was not attempting to establish unexpected results for the

tazarotene/high potency corticosteroid over the tazarotene/mid-potency corticosteroid combination, but was showing that the tazarotene/corticosteroid combination as a whole, regardless of potency, is unexpectedly beneficial as compared to tazarotene treatment alone. The proper comparison is not the relative adverse events for the two combinations, but the reduction in adverse events for the combination treatments as compared to tazarotene treatment alone.

In the parent application, and in previous communications, the Office and the Board have consistently pointed to natural variation in a single experimental value to dismiss Applicant's assertion of unexpected results, while ignoring general trends. The statement "the incidence of treatment related adverse events for tazarotene plus mid- or high-potency corticosteroid as taught by Gollnick is almost identical, i.e., 32% and 31% respectively" is a typical example of this. The comparison of mid- to high-potency corticosteroid combinations is part of a data series in the Gollnick reference that states "[t]he incidence of treatment-related adverse events decreased with increased corticosteroid potency, falling from 42% in the taz/plac group to 36%, 32%, and then 31% in the taz/low, taz/mid, and taz/high groups, respectively." These results clearly point to two conclusions. First, that the addition of a corticosteroid to tazarotene therapy reduces adverse events. All three corticosteroids tested in combination with tazarotene had fewer side effects than tazarotene alone. Second, there is a general trend of decreasing adverse events when increasing the potency of the steroid. The statement in the Office Action ignores the general trend and asserts that two isolated data points are contrary to this trend. Applicant does not believe this is a proper analysis of the data.

Further, the Office Action stated that "[o]ne of the major reasons for combination therapy is reduction in adverse reaction of single therapy. *Combination therapy results in the reduction in the amount of each of the drugs therein.*" Applicant would like to clarify that this is not the case in any study done in the present application or in the Gollnick reference. The specification (p. 10, lines 18-25) states "Topical applications of tazarotene 0.1% gel, were administered every other evening, and one of the following creams were administered on alternate evenings: *placebo*; low-potency corticosteroid..." In the study reported in the application, the only difference between the monotherapy group and the

combination therapy groups is that the monotherapy patients received a placebo in place of a dose of corticosteroid. Therefore, the monotherapy group received the same amount of tazarotene as the combination group. Similarly, in the Gollnick reference, patients received an evening dose of tazarotene and a morning dose of corticosteroid or control (p. 19), or tazarotene on alternating days to corticosteroid or placebo (p. 19-20). Thus, there was no reduction in the amount of tazarotene administered for the combination treatments, and the statement "combination therapy results in the reduction in the amount of each of the drugs therein" cannot be correctly applied to the unexpected results asserted by Applicant.

Further Applicant submits herewith an affidavit under 37 C.F.R. § 1.132, signed by a dermatologist, which says the following.

Based upon the evidence in United States Patent Application Serial Number 10/820,298 and in H. Gollnick and A. Menter *British Journal of Dermatology* 1999; 140 (Suppl. 54): 18-23, there appears to be a general trend that combinations of tazarotene and corticosteroids increase efficacy in the treatment of psoriasis while reducing the adverse events as compared to tazarotene alone.

It is generally unexpected that a treatment would increase efficacy while reducing adverse events.

It is generally expected that administering two drugs to a patient will increase the adverse effects as compared to administering either of the individual drugs to the patient, where the dose of the individual drug is the same for individual and combination therapy.

Further, based upon the same evidence, there appears to be a trend of reduction in adverse events for the combination treatment of tazarotene and corticosteroid as the potency of the corticosteroid is increased.

It is generally expected that increasing the potency of a corticosteroid will increase the adverse events.

Finally, based upon said evidence, increased efficacy and reduced adverse events relative to 0.1% tazarotene gel treatment alone for the following combinations is observed: 0.1% tazarotene gel plus 0.1% mometasone furoate; 0.1% tazarotene gel plus 0.05% fluocinonide; 0.1% tazarotene gel plus 0.05% alclometasone dipropionate; and

0.1% tazarotene gel plus 0.1% betamethasone valerate. This combination of increased efficacy and reduced adverse events is unexpected.

The unexpected results supported by the affidavit combined with the points made herein are sufficient to overcome any prima facie case of obviousness the Office believes may exist. Thus, Applicant believes that the claims are patentable as they now stand, and respectfully requests that Examiner pass them to issue.

Respectfully submitted,



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Date: February 8, 2005

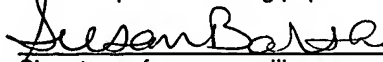
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CERTIFICATE OF EXPRESS MAIL UNDER 37 C.F.R. §1.10

I hereby certify that this Preliminary Amendment and the documents referred to as enclosed herein are being deposited with the United States Postal Service on **FEBRUARY 8 2005** in an envelope as "Express Mail Post Office To Addressee" mailing label number **EV295681885US** with sufficient postage for Express Mail addressed to Mail Stop: Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Susan Bartholomew
Name of person mailing paper


Signature of person mailing paper

Date: February 8, 2005